

Anthrax vaccination in a military population before the war in Iraq: Side effects and informed choice

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Received 27 April 2007; received in revised form 13 August 2007; accepted 26 August 2007

Available online 19 September 2007

Abstract

Background: To assess any health consequences of the anthrax vaccination programme in UK Armed Forces deployed to Iraq.

Methods: Data were collected from two samples simultaneously. The first was 5302 randomly selected UK service personnel. The second was 607 service personnel involved in a longitudinal study, where pre-vaccination health had previously been collected. Both samples were offered the anthrax vaccination before they deployed to Iraq in 2003 and subsequently following their service in Iraq. Participants completed a detailed questionnaire, including a range of health outcomes, receipt of the anthrax vaccination and quality of choice.

Results: Seventy-two percent of the combined sample had the anthrax vaccination. Being a member of the Army, a commissioned officer or a reservist was associated with higher uptake. No differences in self-reported health were observed between those who did and did not receive the vaccination. For participants who accepted the vaccination, we found an association between making an uninformed choice and adverse health. After adjustment for baseline health in the longitudinal cohort these associations remained significant.

Conclusions: Anthrax vaccination used by the UK Armed Forces in preparation for the Iraq War has not resulted in adverse health outcomes. However, of those who did accept the vaccination, reported side effects were related to whether acceptance of vaccination was perceived to be informed. Improving the quality of choice may improve self-reported ill health.

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Keywords: Anthrax vaccination; Informed choice; Side effects; Gulf War syndrome

1. Introduction

Vaccination safety has become an increasing cause of public anxiety, triggered in part by the Measles, Mumps and Rubella (MMR) vaccination crisis. This has contributed to, and was symptomatic of, a general scepticism towards vaccination. Concurrent with this general anxiety about vaccinations is a focus on risk rather than benefit in public discussion about vaccination, resulting in greater emphasis being placed on the concept of informed choice [1].

The 1991 Gulf War (GW), and subsequent ill health of service personnel [2–4], created an atmosphere within the

military not dissimilar to that caused by the MMR crisis in the general population. Following the Gulf War, many veterans reported poorly defined illnesses, and many veterans as well as the media, attributed these to the anthrax vaccination [5]. Two epidemiological studies linking the use of anthrax vaccination to symptomatic ill health in GW veterans showed a modest (OR = 1.4 and 1.5) association between self-reported anthrax vaccination and multiple physical symptoms [2,6]. Such findings, however, have not been replicated in subsequent studies, where the participants were not limited to GW veterans [7–10].

In the build-up to the 2003 Iraq War, the UK Ministry of Defence (MoD) offered the anthrax vaccination as part of the preparation of service personnel prior to deployment. The anthrax vaccination was offered on a voluntary basis

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supported by a Vaccine Information Programme (Voluntary Immunisation Programme), which consisted of video and written information, intended to facilitate informed choices. Personnel were then given a “cooling off” period before being invited to sign a consent form. This move reflected changes in society away from medical paternalism and towards medical consumerism, underpinned by informed choice, and was intended to increase confidence in the anthrax vaccination programme. It was also a response to the problems associated with the vaccination following the 1991 Gulf War. However, in a previous paper we identified that the voluntary policy may have instead increased concerns and failed to address the negative health associations that were perceived to exist [11]. The full vaccination programme consists of four injections and an annual booster. The administration of the anthrax vaccinations was spaced-out with typically 2/3 weeks between injections. Service personnel also received other routine vaccinations (e.g. tetanus, typhoid, yellow fever and hepatitis A). Whilst these were administered over the same time period in preparation for the 2003 Iraq War, other vaccinations were not administered on the same day as the anthrax vaccination.

1.1. Aims

The aims of this paper were: to test the hypothesis that the vaccination is associated with adverse health outcomes; to determine whether uninformed choice to receive anthrax vaccinations is associated with health outcomes; and, with a second sample of individuals, to control for pre-vaccination health to reduce confounding by negative affect.

As computerised anthrax vaccination records were incomplete we assessed the level of agreement between self-reported and recorded anthrax vaccination to decide the appropriateness to use self-reported information on vaccination in the analysis. We have used a definition of informed choice supported by research that has identified three aspects: knowledge, attitude, and the congruence between actual choice and behaviour [12]. Given this perspective an informed choice is defined as one that is based on relevant knowledge, consistent with the decision-maker's values and behaviourally implemented.

2. Methods

We carried out this study with two cohorts: an Iraq War and a screening cohort.

2.1. Iraq War cohort

We conducted a cross-sectional study of UK Armed Forces personnel. Two groups were randomly selected: individuals who had deployed to the first phase of the Iraq War (Operation TELIC 1), and a control population who were serving at the time but did not deploy on this operation which we labelled “ERA”. Subsequent to the populations being defined, many of

the ERA cohort deployed on later TELIC operations in Iraq. We have restricted our analysis to those personnel who had deployed on any Operation TELIC, which we have defined as our Iraq War cohort. These individuals had all been offered the anthrax vaccination under identical consent procedures. A detailed description of the sampling, stratification and methods employed for contacting respondents for the Iraq War cohort can be found elsewhere [13]. Participants were provided with information about the study and were informed that it was voluntary and that they could withdraw at any stage.

Between June 2004 and March 2006 participants were asked to complete a detailed questionnaire including questions regarding vaccination uptake, level of informed choice to accept or decline the anthrax vaccination, side effects directly attributed to the vaccination and in a separate section not dealing with vaccinations a range of health outcomes. Physical symptoms were recorded using a 53-item checklist [2], symptoms of common mental disorder were measured using the General Health Questionnaire 12 (GHQ-12) [14], fatigue was assessed using a 13-item fatigue scale [15], self-perception of health was measured using a single item from the SF-36 (‘In general, how would you rate your health?’, Poor/Fair/Good/Very Good/Excellent) [16], and symptoms of post-traumatic stress disorder (PTSD) were measured using the 17-item National Centre for PTSD checklist (PCL-C) [17]. The criteria for case definitions were 4 items or above on the GHQ-12 and fatigue scales, rating health as “poor” or “fair”, a score of 50 or more on the PCL-C, 11 or more, and 18 symptoms or more (above the 75th and 90th percentile). We used two cut-offs in our assessment to provide an overview related to number of symptoms as a proxy measure of severity. Informed choice was measured using three items adapted from the Ottawa Conflict Decision Scale [18]. Participants were defined as making an informed choice if they did not feel pressure to accept the vaccination; were satisfied with their decision; and would repeat their decision in the future (if they accepted the vaccination, they would do so again if offered, and vice versa). The informed choice variable had a moderately high Cronbach's alpha of 0.61.

2.2. Screening cohort

In 2002, we conducted a study to test the feasibility of screening to assess psychological health in the UK Armed Forces. Two groups were randomly selected to receive either a full or an abridged questionnaire. The three services were represented by their relative strength at July 2001. Units (regiments, ships, etc.) were randomly selected, and 45 individuals were randomly selected from each unit. After taking into account those participants without a valid address the response rate was 67% ($n = 2873$). Further details are reported elsewhere [19]. Subsequent to the invasion of Iraq, between June 2004 and March 2006, 2730 of these participants were invited to complete a second questionnaire. This follow-up study was conducted simultaneously with the Iraq War cohort

as described above [13]. It therefore offered an opportunity to look at the influence of pre-deployment, and therefore pre-vaccination, psychological variables on post-vaccination health.

In this paper we have restricted our analysis to participants who responded to the follow-up study and went on to deploy to Iraq and who were offered the anthrax vaccination as part of their pre-deployment preparations. The participants in the screening cohort do not overlap with those in the Iraq War cohort.

From the 2002 questionnaire, we used the health outcome measures that were common to both the full and the abridged versions. We elected to use measures common to both questionnaires to maximise our sample size. Participants were asked to complete a range of health outcomes. These included an assessment of health status using a single item from the SF-36 [16] (“in general, how would you rate your health? Poor/Fair/Good/Very Good/Excellent”), five-item symptom checklist selected from a previously used questionnaire [2], and symptoms of common mental health disorders were measured on using four items from the General Health Questionnaire (GHQ-4) [14]. The criteria for case definitions were two items or above on the GHQ-4, rating health as “poor” or “fair”, and scoring three mild or combinations of mild and moderate or at least one severe symptom on the five-item symptom checklist.

2.3. Assessing agreement between medical records and self-reported uptake of anthrax vaccination

Complete electronic vaccination records for all three services do not exist, so agreement between self-reported anthrax vaccination uptake and paper medical records was assessed. We decided to assess agreement in 10% of our sample. A sub-sample of approximately 12% was selected, stratified by service and rank, all of which had given consent to access their medical records. A member of the research team (DM) visited military medical centres and collected data on anthrax vaccination uptake, for the period 31 July 2002–31 June 2003. To avoid missing data, deployment medical records (which are updated with vaccinations administered during deployment) were requested in addition to standard medical records (‘FMed 4’).

2.4. Analysis

Kappa statistics were used to assess level of agreement between self-reported and documented vaccine uptake. For the Iraq War cohort, multivariable logistic models were fitted to identify demographic variables associated with anthrax vaccination uptake and making an uninformed choice. Logistic regression was used to calculate odds ratios and 95% confidence intervals in assessing the association between health outcomes and anthrax vaccination uptake. For participants who had the vaccination, odds ratios were generated for the association between uninformed choice and health out-

comes. Analyses using the Iraq War cohort were weighted to take into account sampling fractions.

Within the screening cohort comparison was made between baseline health and later anthrax vaccination uptake. Follow-up health and uptake were then assessed controlling for baseline health. We compared baseline health and later quality of informed choice to undergo vaccination and finally, we assessed associations between making uninformed choice to undergo vaccination and reported adverse health, controlling for baseline health.

Analyses were adjusted for service (Naval Services, Army and RAF), rank (whether officer or not), gender, age, medical fitness and enlistment status (regular or reserve) and were conducted using STATA 9 (Stata Corporation, College Station, TX, USA).

3. Results

3.1. Agreement between self-reported uptake of anthrax vaccination and medical records

Six hundred and thirty-two records were selected. The research team were able to access 507 records (80%). Hundred and twenty-five records were unavailable for individuals who had been posted to other bases or who had left service. Substantial agreement (Kappa=0.81; 95% CI 0.73–0.90) was found between questionnaire self-report and written medical records recording anthrax vaccination. We found a level of agreement of 92%. The positive agreement for accepting the vaccination was 95%, and the negative was 86%, thus justifying the use of self-reported vaccination in the analysis.

3.2. Iraq War cohort

Ten thousand two hundred and seventy-two (61%) of the contacted sample responded to the questionnaire, of whom 5302 participants were assigned to our Iraq War cohort and included in these analyses. Hundred and sixty (0.9%) refused to participate in the study. Of the responders, 13% were in the Naval Services, 68% Army and 19% Royal Air Force (RAF). Nine percent of the samples were female, 17% commissioned officers and 17% reservists. The median age was 32.2 years (inter-quartile range 26.4–38.2). In an intensive follow-up study of non-responders already reported, non-response was largely due to our difficulty in finding people or participant inertia, with no significant differences between responders and non-responders in terms of health [13]. Furthermore, there was no significant difference in rates of medical “downgrading” (a measure of general overall health) between responders and non-responders [20].

3.2.1. Comparison of those who took the anthrax vaccination and those who did not

Three thousand eight hundred and twenty-one (72%) had the anthrax vaccination. The Army coverage was 78%, for

Table 1
Factors associated with receiving the vaccination (anthrax vaccine uptake = 72.1%)

	No anthrax vaccine		Anthrax vaccine		OR	95% CI	Adjusted odds ratio ^a	
	<i>n</i>	(%) ^b	<i>n</i>	(%) ^b			OR	95% CI
Service								
Naval Services	295/713	(42)	418/713	(58)	1.00		1.00	
Army	764/3588	(22)	2824/3588	(78)	2.56	2.16–3.04	3.90	3.24–4.70
RAF	422/1001	(43)	579/1001	(57)	0.94	0.77–1.15	1.11	0.90–1.37
Rank								
Ranks	1311/4420	(31)	3109/4420	(69)	1.00		1.00	
Officer	170/882	(19)	712/882	(81)	1.84	1.53–2.21	2.32	1.89–2.86
Sex								
Male	1376/4824	(29)	3448/4824	(71)	1.00		1.00	
Female	105/478	(24)	373/478	(76)	1.34	1.07–1.69	1.32	1.02–1.70
Status								
Regular	1317/4400	(30)	3083/4400	(70)	1.00		1.00	
Reservist	164/902	(18)	738/902	(82)	1.92	1.60–2.30	1.75	1.42–2.16
Age								
Per 10 years	32.1 years	Median	32.3 years	Median	0.98	0.90–1.06	0.88	0.79–0.97

^a Adjusted for service, rank, sex, regular/reservist status, age 10.

^b Percentages adjusted to take account of sampling fractions.

the Naval Services 58% and for the RAF 57%. Anthrax vaccination uptake was significantly associated with being, in the Army, an officer, female or a reservist (Table 1).

3.2.2. Description of health effects associated with anthrax vaccination uptake

No significant differences were observed in the self-reported health outcomes between those who had the anthrax vaccination and those who did not, except for multiple symptoms (Table 2). We found no association when the cut-off was 11 (OR 1.09; 95% CI 0.94–1.26) but did when the cut-off was 18 (1.36; 1.10–1.69). The positive association between reporting 18 or more symptoms and having anthrax vaccination disappeared when we adjusted for informed choice (1.00; 0.80–1.25).

3.2.3. Factors predicting making an uninformed choice to undergo vaccination

Four thousand one hundred and ninety-two (79%) participants reported making an informed choice regardless of their

decision to undergo vaccination or not. Of those who were vaccinated, 2728 (71%) reported making an informed choice to have the vaccination, compared to those who decline 1464 (99%). In a multivariable logistic regression model, after adjustment being in the Army and being female were identified as predictors of uninformed choices (Table 3). Factors that reduced the likelihood of making an uninformed choice were being an officer, and being older.

3.2.4. Impact of informed choice on health

These analyses were restricted to participants who chose to be vaccinated. Table 4 shows that participants who made uninformed choices reported worse health on a range of outcomes. They were more likely to rate their health as “fair” or “poor”, report 11+ or 18+ symptoms, and score above the cut-offs on the GHQ-12, fatigue and PCL-C scales.

3.3. Screening cohort

One thousand eight hundred and eighty-five (67%) of the 2730 sample, first contacted in 2002, responded to the follow-

Table 2
Self-reported health comparisons between those who had and did not have anthrax vaccination

	No anthrax vaccine		Anthrax vaccine		Unadjusted odds ratio		Adjusted odds ratio ^a	
	<i>n</i>	(%) ^b	<i>n</i>	(%) ^b	OR	95% CI	OR	95% CI
Fatigue case	457/1467	(31)	1292/3758	(34)	1.14	0.99–1.30	1.04	0.90–1.19
GHQ-12	282/1471	(19)	783/3774	(20)	1.09	0.93–1.27	1.03	0.87–1.22
PCL-C	62/1463	(4)	162/3759	(4)	1.06	0.88–1.29	0.90	0.65–1.25
Health perception	163/1475	(11)	453/3797	(11)	1.01	0.74–1.37	1.00	0.81–1.23
Multiple physical symptoms								
11+	400/1481	(27)	1179/3821	(30)	1.17	1.03–1.35	1.09	0.94–1.26
18+	144/1481	(10)	509/3821	(13)	1.41	1.15–1.72	1.36	1.10–1.69

^a Adjusted for age 10, sex, service, rank, fitness to deploy and regular/reservist status.

^b Percentages adjusted to take account of sampling fractions.

Table 3
Factors associated with making an uninformed choice to undergo vaccination

	Made informed choice		Made uninformed choice		Unadjusted odds ratio		Adjusted odds ratio ^a	
	<i>n</i>	(%) ^b	<i>n</i>	(%) ^b	OR	95% CI	OR	95% CI
Service								
Naval Services	602/713	(84)	111/713	(16)	1.00		1.00	
Army	2720/3588	(75)	868/3588	(25)	1.71	1.37–2.12	1.67	1.34–2.09
RAF	870/1001	(87)	131/1001	(13)	0.80	0.61–1.05	0.86	0.65–1.13
Rank								
Ranks	3430/4420	(77)	990/4420	(23)	1.00		1.00	
Officer	762/882	(86)	120/882	(14)	0.55	0.45–0.68	0.65	0.52–0.81
Sex								
Male	3835/4824	(79)	989/4824	(21)	1.00		1.00	
Female	357/478	(74)	121/478	(26)	1.37	1.09–1.71	1.42	1.12–1.79
Status								
Regular	3454/4400	(79)	946/4400	(21)	1.00		1.00	
Reservist	738/902	(82)	164/902	(18)	0.81	0.67–0.98	0.91	0.74–1.11
Age								
Per 10 years	32.7 years	Median	30.3	Median	0.68	0.62–0.75	0.77	0.70–0.86

^a Adjusted for age 10, sex, service, rank, fitness to deploy and regular/reservist status.

^b Percentages adjusted to take account of sampling fractions.

up questionnaire. A more detailed description of response rates is described by Rona et al. [19]. Forty-four (1.6%) individuals refused to participate. The sample used for this paper consisted of 607 participants who had deployed to Iraq since 2003 and been offered the anthrax vaccination as part of their preparations. Of these 22% were officers and 93% male. Thirteen percent were in the Naval Services, 53% in the Army and 34% in the RAF. The median age was 34.4 years (inter-quartile range 30.1–38.8).

3.3.1. Comparisons between uptake of anthrax vaccination and health

Assessments between baseline health outcome, pre-vaccination, and vaccination uptake are described in Table 5. No differences in pre-vaccination health were observed. In the assessment of health following vaccination, a similar pat-

tern emerged, with no differences in the health between those who received the anthrax vaccination and those who did not.

3.3.2. Impact of informed choice on health

We assessed possible associations between baseline health measures and quality of informed choice to undergo vaccination. Scoring above the pre-defined cut-offs on the GHQ-4 and the symptom checklist in 2002 was associated with subsequently reporting making an uninformed choice to receive the anthrax vaccination (Table 6). Two models were used to assess associations between follow-up health and quality of informed choice (Table 6). The first model replicated the analyses above with the Iraq War cohort, assessing associations between informed choice and health adjusted for socio-demographic factors. A similar pattern of results was observed. Making an uninformed choice to receive the

Table 4
Self-reported health comparisons between those making an uninformed choice and informed choice to accept the anthrax vaccination

	Made informed choice		Made uninformed choice		Unadjusted odds ratio		Adjusted odds ratio ^a	
	<i>n</i>	(%) ^b	<i>n</i>	(%) ^b	OR	95% CI	OR	95% CI
Health outcomes								
Fatigue case	803/2685	(29)	489/1073	(45)	2.02	1.74–2.35	1.99	1.70–2.32
GHQ-12	465/2699	(16)	318/1075	(29)	2.11	1.78–2.49	2.09	1.76–2.48
PCL-C	83/2688	(3)	79/1071	(7)	2.58	1.86–3.57	2.23	1.59–3.14
Health perception	251/2710	(9)	202/1087	(18)	2.35	1.91–2.89	2.49	1.99–3.12
Multiple physical symptoms								
11+	700/2728	(25)	479/1093	(44)	2.36	2.03–2.75	2.40	2.05–2.81
18+	273/2728	(10)	236/1093	(21)	2.53	2.08–3.08	2.47	2.01–3.03
Attributed to vaccine								
Flu-like	1139/4192	(42)	698/1110	(64)	2.53	2.18–2.94	2.53	2.17–2.95
Sore arm	1700/4192	(62)	810/1110	(74)	1.74	1.49–2.04	1.69	1.43–1.99
Other side effects	172/4192	(6)	193/1110	(18)	3.59	2.85–4.52	3.57	2.81–4.54

^a Adjusted for age 10, sex, service, rank, fitness and regular/reservist status.

^b Percentages adjusted to take account of sampling fractions.

Table 5

Associations between baseline health and receipt of anthrax vaccination and between follow-up health and anthrax vaccination uptake, adjusted for baseline health

	No anthrax vaccine		Anthrax vaccine		Unadjusted OR		Model 1 ^a		Model 2 ^b	
	<i>n</i>	(%)	<i>n</i>	(%)	Odds	95% CI	Odds	95% CI	Odds	95% CI
Baseline health										
GHQ-4	41/238	(17)	68/369	(18)	1.09	0.71–1.66	1.06	0.69–1.65		
Health perception	23/238	(10)	42/369	(13)	1.20	0.71–2.05	1.15	0.66–1.99		
Physical symptoms	31/238	(13)	61/369	(17)	1.32	0.83–2.11	1.26	0.78–2.05		
Follow-up health										
Fatigue	65/237	(27)	121/366	(33)	1.31	0.91–1.87	1.29	0.90–1.87	1.26	0.86–1.83
GHQ-12	40/238	(16.8)	73/369	(19.8)	1.22	0.80–1.87	1.27	0.82–1.97	1.25	0.79–1.98
Physical symptoms										
11+	62/238	(26)	117/369	(31.7)	1.32	0.92–1.90	1.31	0.90–1.90	1.28	0.86–1.91
18+	20/238	(8.4)	38/369	(10.3)	1.25	0.71–2.21	1.18	0.66–2.10	1.04	0.55–1.97

^a Adjusted for age 10, sex, service, rank, regular/reservist status and fitness to deploy.

^b Adjusted for variables in Model 1 and baseline health (GHQ-4, health perception and physical symptoms).

anthrax vaccination was significantly associated with reporting worse health on a range of health outcomes. These findings may be limited due to influences of recall bias, in which poor health leads to a perception that choices made were uninformed. We have found support for this from the analyses shown in Table 6 where significant associations were found between adverse baseline health and later making an uninformed choice. After adjustment for baseline health and socio-demographics, those making an uninformed choice to undergo anthrax vaccination reported significantly more common symptoms of mental ill health (GHQ-4) and more symptoms of fatigue.

4. Discussion

In the Iraq War cohort, there were three principal findings. First, there was substantial agreement between self-reported vaccination and vaccination records; secondly, after adjustment, no association was found between anthrax vaccination and adverse health for five of our six health outcomes, and

thirdly, making a perceived uninformed choice was associated with both reported side effects directly associated with the vaccination and more general subjective health outcomes. In addition to these principal findings we were, with the screening cohort, able to examine the effect of pre-vaccination health. Differences in pre-vaccination health were observed between those individuals who later made informed and those who made uninformed choices to receive the vaccination. Worse pre-vaccination health was associated with later making an uninformed choice to undergo vaccination. This may have reflected differences in negative affect (NA) between individuals. Individuals who reported making uninformed choices may have had higher levels of NA and hence reported worse health. Our findings suggest that, when we control for confounding by NA, there is still a significant association between making an uninformed choice to undergo vaccination and adverse health. It was observed that receipt of the anthrax vaccination was associated with being younger, in the Army, female, an officer or a reservist. We interrupt being younger and in the Army as representing the infantry troops who were frontline and may have seen them-

Table 6

Associations between baseline health and making an uninformed choice and between follow-up health outcomes and making an uninformed choice, adjusted for baseline health

	Informed choice		Uninformed choice		Unadjusted OR		Model 1 ^a		Model 2 ^b	
	<i>n</i>	(%)	<i>n</i>	(%)	Odds	95% CI	Odds	95% CI	Odds	95% CI
Baseline health										
GHQ-4	83/506	(16)	26/101	(26)	1.77	1.07–2.92	1.67	1.00–2.79		
Health perception	50/506	(10)	15/101	(15)	1.59	0.85–2.96	1.33	0.70–2.53		
Physical symptoms	67/506	(13)	25/101	(25)	2.16	1.28–3.62	2.01	1.18–3.44		
Follow-up health										
Fatigue	141/505	(28)	45/98	(46)	2.19	1.41–3.41	2.13	1.36–3.35	1.91	1.20–3.04
GHQ-12	83/506	(16)	30/101	(30)	2.15	1.32–3.51	2.14	1.30–3.54	1.91	1.13–3.23
Physical symptoms										
11+	140/506	(28)	39/101	(39)	1.64	1.05–2.57	1.62	1.03–2.55	1.36	0.83–2.23
18+	41/506	(8)	17/101	(17)	2.30	1.25–4.23	2.08	1.11–3.89	1.73	0.86–3.49

^a Adjusted for age 10, sex, service, rank, regular/reservist status and fitness to deploy.

^b Adjusted for variables in Model 1 and baseline health (GHQ-4, health perception and physical symptoms).

selves as more at risk, officers may have felt a need to set an example and reservists may have felt more at risk than their regular counterparts. The higher uptake in women is intriguing; this may be accounted for by previously documented increased likelihood of health seeking behaviour by women [21,22].

The study had several strengths. The sample was representative of the wider Armed Forces, including all three services, both officers and other ranks, and serving and ex-serving personnel. We were able to ensure that the use of self-reported uptake of anthrax vaccination was highly reliable. This was supported by research with the Millennium cohort that found a similarly high level of agreement between self-reported receipt of the anthrax vaccination and medical records ($\kappa=0.80$) [23]. The collection of longitudinal data for the screening cohort meant we had both pre- and post-vaccination health data. This allowed us to use differences in pre-vaccination health between individuals who made informed and uninformed choices as a proxy measure for NA. In addition, pre-vaccination health was measured without any reference to anthrax vaccination or choice. In the follow-up questionnaire the measure of anthrax vaccination uptake and choice was embedded in a section of the questionnaire concerned with deployment experiences whilst the questions pertaining to health were in a later unrelated section. This was an advantage because previous studies have found that individuals with higher NA were more likely to over report symptoms by misinterpreting common symptoms as resulting from the intervention being studied [24,25]. Having questions about anthrax vaccination and health in separate sections may have minimised any framing effect as the health measures were not linked to the questions about vaccination. Importantly, the anthrax vaccination was offered to all participants at around the same time and under identical consent procedures.

A limitation of this paper is the reliance on retrospective data for measures of choice. Whilst the design of the study allowed adjustment for pre-vaccination health, as a proxy measure of NA, the ideal would have been to measure quality of choice at the time of vaccination. This was however logistically impossible during the preparations for the 2003 war. We were not able to identify the reasons for refusing the anthrax vaccination. In a previous paper we identified that concerns about the anthrax vaccination were prevalent which may go some way to explain refusal rates.

The study was conducted soon after a change of policy from traditional medical paternalism to offering the vaccination on an explicitly voluntary basis with informed choice. The aim behind the change in policy was to increase confidence and uptake in the anthrax vaccination programme. We have already suggested that singling out one vaccination for special attention (as opposed to all the other vaccinations routinely used by the Armed Forces) may have increased concerns for some, damaging trust and not addressing the context surrounding vaccination [11].

Anthrax vaccination coverage was generally high, with coverage for the Army highest, showing that before the Iraq War the threat of biological weapons was taken seriously. Our findings show no significant increase in adverse health outcomes in those who received anthrax vaccinations compared to those who did not, except when we used a cut-off of 18 physical symptoms or more. We interpret this latter finding as fortuitous because the effect size was small; it disappeared after adjustment for informed choice, it was inconsistent with the lack of association when we used a cut-off of 11 or more symptoms, and was the only significant association out of 6 comparisons.

Our findings contrast with other studies that reported an association between physical symptoms and vaccination in GW veterans [2,6], but are in agreement with other studies not limited to GW veterans [7–10,21]. What accounts for these differences is unclear. Data for this study were collected between 1 and 3 years after the war in Iraq, whilst the GW studies did not commence until 5–10 years after the end of hostilities. Continued study of the 2003 population is needed to rule out long-term adverse health effects. The combination of anthrax and plague, with pertussis as an adjuvant, given to UK personnel prior to the 1991 Gulf War differed from that given to personnel deployed in the 2003 Iraq conflict; the 2003 vaccination programme was administered without pertussis as an adjuvant, and the four injections were more spaced out. The role of multiple vaccinations on ill health remains contentious. Some evidence from the 1991 GW suggested a weak association with increased symptomatic ill health [26]. In a further paper we will be investigating the pattern of health outcomes as a result of self-reported or actual multiple vaccines received.

Health outcomes were related to how people perceive the vaccination, and in particular how informed their choices were to accept the vaccination. The introduction of prostate screening in America provides an example of a policy that was changed to encourage informed choice, but instead has caused increased levels of anxiety, concurrent with increased numbers being screened [27]. Evidence from cancer patients has shown that a lack of relevant information may lead to anxiety [28]. Individuals who have high anxiety levels report greater sensitivity to symptoms following medical interventions [29].

5. Conclusions

To date, there has been no adverse health outcomes observed in UK service personnel who received the anthrax vaccination since the 2003 Iraq War. However, participants who made an uninformed choice to be vaccinated reported worse health outcomes. The mechanism for these associations is unknown. We hypothesised that those who felt dissatisfied or badly informed with the decision to accept anthrax vaccination are more prone to develop a feeling of ill health. Making uninformed choices may have increased anx-

ity, symptom amplification and sensitivity, which may have caused the increase in reported adverse health. Whether these associations will disappear if informed choices are facilitated more effectively for all those offered vaccinations requires evaluation.

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